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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,674	08/03/2000	ALBERTO A. GABIZON	9325-0007.10	8870

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BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER

WEBER, JON P

ART UNIT

PAPER NUMBER

1651

DATE MAILED: 12/18/2002

25

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/555,674

Applicant(s)

GABIZON ET AL.

Examiner

Jon P. Weber, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 54,56,58,60,62,64,66,68,70,72,74,76,78,80,82,84,86,88,90 and 92 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 54,56,58,60,62,64,66,68 and 70 is/are allowed.
- 6) ☒ Claim(s) 72,74,76,78,80,82,84,86,88,90 and 92 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 23.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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Status of the Claims

Claims 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78 80 82, 84, 86, 88, 90 and 92 have been presented for examination.

Reopening Prosecution

The Notice of Allowability mailed 09 September 2002 is hereby withdrawn in view of the new grounds of rejection *infra* based upon prior art provided with the IDS of 22 August 2002 but not matched with the file or available for consideration by examiner at the time of mailing of the Notice of Allowability. The time period for response is hereby reset to begin with the date of mailing of this Office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 72, 74, 76, 78 80 82, 84, 86, 88, 90 and 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ostro (EP 546,951) in view of Kedar et al. (1994).

The claims are drawn to a combination therapy for treating neoplasms comprising administration of a liposome encapsulated antineoplastic drug followed by administration of two or more doses of MLV encapsulated cytokines at least three days after administering the drug.

Ostro (EP 546,951) discloses a combination therapy for treating neoplasms comprising administration of a liposome or MLV encapsulated antineoplastic drug followed by

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administration of several doses of hematopoietic cell stimulating cytokine beginning on the fourth day after drug administration (Example 3). The preferred cytokine is G-CSF, but the hematopoietic cell stimulating agents include other CSFs, **interleukins**, erythropoietin and platelet stimulating factors (page 3, lines 45-47). Suitable antineoplastic drugs are given at page 4, lines 27-36. The lipids that may be used for the liposomes are disclosed at page 5, line 58 to page 6, line 17. At page 7, lines 20-23, it is stated that the hematopoietic cell stimulating agent may be administered by any method known in the art, such as a pharmaceutically acceptable carrier or diluent. Ostro (EP 546,951) lacks administering the cytokines in MLVs.

Kedar et al. (1994) disclose that the advantages of administering cytokines in MLVs compared to free in solution for the therapeutic treatment of neoplasms include decreased clearance time, controlled delivery, protection from inactivating enzymes and antibodies, and versatility in formulation of the liposomes and dosages. At page 48, in the paragraph bridging the two columns, reference is made to findings that show that SSL liposome encapsulated cytokines have superior antitumor effects compared to non-encapsulated soluble cytokines.

A person of ordinary skill in the art at the time the invention was made would have been motivated to substitute the MLV encapsulated cytokines of Kedar et al. (1994) for non-encapsulated cytokines in the method of Ostro (EP 546,951) because of the various advantages of the encapsulated cytokines over non-encapsulated cytokines including enhanced antitumor effects disclosed by Kedar et al. (1994). The liposomes of Kedar et al. (1994) are well known pharmaceutically acceptable carriers within the scope of administration methods suggested by Ostro (EP 546,951).

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Then selection of specific lipids or specific ratios of lipids within the MLVs is within the skill of the ordinary artisan to select and optimize. The formation of liposomes and MLVs is a well developed art as discussed in both Ostro (EP 546,951) and Kedar et al. (1994). In particular, the SSL or stealth liposomes, are particularly advantageous according to Kedar et al. (1994).

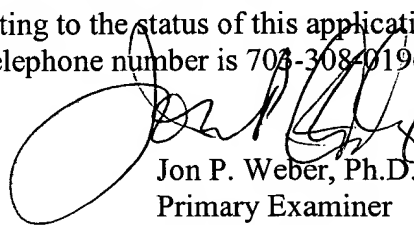
Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the MLV encapsulated cytokines of Kedar et al. (1994) for non-encapsulated cytokines in the method for treating neoplasms of Ostro (EP 546,951).

Claims 54, 56, 58, 60, 62, 64, 66, 68 and 70 remain allowed there being no reason or basis to remove the liposomes from the therapeutic drug in the method of Ostro (EP 546,951). The point in Ostro (EP 546,951) is to provide the therapeutic drug in a liposomal carrier. Hence, Ostro (EP 546,951) teaches away from removing the liposomes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P. Weber, Ph.D. whose telephone number is 703-308-4015. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-40196.



Jon P. Weber, Ph.D.
Primary Examiner
Art Unit 1651

JPW
December 13, 2002